Synthesis of Benzo[b]thiophene Carboxamides Connected to 4-Arylpiperazines through a Benzylic Spacer: Potential Ligands with 5-HT\textsubscript{1A} Binding Affinity

Hernán Pessoa-Mahana, R. Acevedo, Ramiro Araya-Maturana, and Claudio Saitz
Faculty of Chemical and Pharmaceutical Sciences, Department of Organic and Physical Chemistry, University of Chile, Santiago, Chile

C. David Pessoa-Mahana
Faculty of Chemical, Department of Pharmacy, Pontificia Universidad Católica de Chile, Santiago, Chile

Abstract: New benzo[b]thiophene arylpiperazine derivatives 8 (a–f) were synthesized as potential serotonergic agents with 5-HT\textsubscript{1A} receptor affinity. Preparation of the derivatives was performed by treating \(N\)-[2-(chloromethyl)phenyl]-4,7-dimethoxybenzo[b]thiophene-2-carboxamide (7) with a series of substituted 4-arylpiperazines.

Keywords: arylpiperazines, benzothiophene, depression, 5-HT\textsubscript{1A}

INTRODUCTION

The long-chain arylpiperazine derivatives provide one of the most universal templates used for designing CNS-active agents, representing the main pharmacophoric fragment recognized for serotonergic, dopaminergic, and adrenergic...
receptors. Compounds of this class have been extensively studied, especially as 5-HT1A receptor ligands, because of their potential antianxiety and antidepressant properties. Among these, some long-chain arylpiperazines with a terminal imide fragment, such as buspirone (I) or ipsapirone (II) (Fig. 1) are effective as antianxiety and antidepressant drugs.

Although a number of synthetic approaches to long-chain arylpiperazines with interesting 5-HT1A bioactivity have been reported, the preparation of arylpiperazinyl benzothiophene derivatives (III) with a benzylic spacer inserted between the basic nitrogen atom of the arylpiperazine moiety and the benzo[b]thiophene carboxamide nucleus, as far as we know, has not yet been investigated.

In this article, the synthesis of a series of 4,7-dimethoxy-N-{2-[4-aryl-1-piperazinyl] methyl}phenyl]benzo[b]thiophene-2-carboxamides of general structure (III) closely related to bioactive long-chain arylpiperazines is reported (Fig. 1).

RESULTS AND DISCUSSION

The new compounds 8(a–f) were synthesized from the aroyl benzothiophene (5) according to the sequence displayed in Scheme 1. The preparation of (5) was carried out in three steps from the previously described 2-nitrobenzaldehyde (1), which was converted to ester (3) by treatment with methyl thioglycolate in basic medium. The mechanism of the cyclization of the 2-nitrobenzaldehyde derivative is unknown. However, a reasonable mechanism probably involves thiol anion displacement of the activated nitro group followed by base-catalyzed aldol-condensation to afford (3). Subsequent basic hydrolysis of (3) to acid (4) followed by treatment with thionyl chloride under reflux conditions afforded compound (5) (Scheme 2).
The aroylchloride (5) was purified and reacted with 2-aminobenzyl alcohol under inert conditions to give the corresponding amide (6) in 89% yield. When (6) was treated with mesyl chloride in the presence of triethylamine, the chlorobenzyl carboxamide (7) in 86%, was obtained instead of the expected mesylate derivative. This product may arise from a nucleophilic attack by chloride on previously formed mesylate under the reaction conditions. In the final step, compound (7) was treated with substituted 4-arylpiperazines under reflux in acetonitrile to provide the expected benzothiophene arylpiperazine carboxamides 8 (a–f) in good yield (65–96%) (Table 1).

Scheme 1. Reagents and conditions: a) 2-aminobenzyl alcohol/dry pyridine/anhydrous THF/N₂ atmosphere; b) mesyl chloride/anhydrous N(Et)₃/dry CH₂Cl₂; c) substituted 4-arylpiperazines/anhydrous K₂CO₃/CH₃CN, reflux.

The aroylchloride (5) was purified and reacted with 2-aminobenzyl alcohol under inert conditions to give the corresponding amide (6) in 89% yield. When (6) was treated with mesyl chloride in the presence of triethylamine, the chlorobenzyl carboxamide (7) in 86%, was obtained instead of the expected mesylate derivative. This product may arise from a nucleophilic attack by chloride on previously formed mesylate under the reaction conditions. In the final step, compound (7) was treated with substituted 4-arylpiperazines under reflux in acetonitrile to provide the expected benzothiophene arylpiperazine carboxamides 8 (a–f) in good yield (65–96%) (Table 1).

Scheme 2. Reagents and conditions: a) methyl thioglycolate/K₂CO₃/DMF, 65–70°C, 4 h. b) KOH–CH₃OH, 3 h, rt, H₃O⁺; c) SOCl₂, reflux, 3 h.
EXPERIMENTAL

Melting points were determined on a hot-stage apparatus and are uncorrected. The IR spectra were recorded on a FT-IR Bruker IFS 55 spectrophotometer for KBr discs, and wave numbers are reported in cm$^{-1}$. The $^1$H NMR and $^{13}$C NMR spectra were performed on a Bruker DRX-300 spectrometer (300 and 75 MHz) in deuteriochloroform, or DMSO-d$_6$. Chemical shifts were recorded in parts per million (ppm δ) relative to TMS as an internal standard. J values are given in hertz. Microanalyses were carried out on a Fisons EA 1108 analyzer. Silica gel Merck 60 (70–230mesh) and DC-alufolien 60 F$_{254}$ were used for column and thin-layer chromatography (TLC) chromatography, respectively.

$N$-[2-(Hydroxymethyl)phenyl]-4,7-dimethoxybenzo[b]thiophene-2-carboxamide (6)

Aroyl chloride (5) (348 mg, 1.36 mmol) in dry THF (20 mL) was slowly added to a stirred solution of 2-aminobenzyl alcohol (168 mg, 1.36 mmol) and dry pyridine (0.11 mL, 108 mg, 1.36 mmol) in dry THF (50 mL) at 0°C under nitrogen atmosphere. After stirring for 10 min, the mixture was allowed to warm to room temperature and was maintained at rt for 3 h. The mixture was then diluted with water (100 mL), extracted with ethyl acetate (3 × 50 mL), and dried over anhydrous Na$_2$SO$_4$. Concentration of the solvent in vacuo afforded the crude amide (6) (415 mg, 89%), which was purified by silica-gel column chromatography (AcOEt/CH$_2$Cl$_2$ 1:2) to afford pure benzothiophene carboxamide (6) (326 mg, 70%) as a brown pale solid. Mp: 150–151°C; anal. calcd. for C$_{18}$H$_{17}$NO$_4$S: C, 62.91; H, 4.99; N, 4.08; S, 9.32. Found: C, 61.95; H, 4.97; N, 4.18; S, 9.28%. IR $v$$_{\text{max}}$: 3350 (ArCONH), 3288 (O-H), 1635 (C=O). $^1$H NMR (300 MHz,CDCl$_3$) δ: 3.86 (s, 6H, 2× ArOMe), 4.55 (d, 2H, Ar-CH$_2$-OH, $\text{J} = 5.3$ Hz), 5.50 (t, 1H, OH, $\text{J} = 5.3$ Hz), 6.83 (d, 1H, 5-H, $\text{J} = 8.5$ Hz), 6.92 (d, 1H, 6-H, $\text{J} = 8.5$ Hz), 7.17–7.27 (m, 2H, 4'-H & 5'-H), 7.41 (d, 1H, 3'-H, $\text{J} = 7.4$ Hz), 7.56 (d, 1H, 6'-H, $\text{J} = 7.7$ Hz), 7.17–7.27 (m, 2H, 4'-H & 5'-H), 7.41 (d, 1H, 3'-H, $\text{J} = 7.4$ Hz), 7.56 (d, 1H, 6'-H, $\text{J} = 7.7$ Hz), 7.17–7.27 (m, 2H, 4'-H & 5'-H), 7.41 (d, 1H, 3'-H, $\text{J} = 7.4$ Hz), 7.56 (d, 1H, 6'-H, $\text{J} = 7.7$ Hz), 7.17–7.27 (m, 2H, 4'-H & 5'-H).
4’-H & 5’-H), 7.41 (d, 1H, 3’-H, J = 7.4 Hz), 7.56 (d, 1H, 6’-H, J = 7.7 Hz),
8.20 (s, 1H, 3-H), and 10.27 (s, 1H, NH-CO). $^1$C NMR (75 MHz, CDCl$_3$): 56.6,
56.8, 61.3, 106.5, 107.9, 123.1, 125.4, 126.3, 128.0, 128.3, 131.23, 131.7,
135.9, 136.4, 139.7, 148.7, 150.5, 160.8.

$^N$-[2-(Chloromethyl)phenyl]-4,7-dimethoxybenzo[b]thiophene-2-
carboxamide (7)

To a solution of alcohol (6) (300 mg, 0.88 mmol) in dry CH$_2$Cl$_2$ (40 mL) at
0°C, mesyl chloride (0.17 mL, 2.2 mmol) and dry Et$_3$N (221 mg, 2.2 mmol)
were added. The mixture was stirred for 3 h at room temperature, diluted
with a saturated solution of NaHCO$_3$ (20 mL), extracted with CH$_2$Cl$_2$
(3 × 50 mL), and dried over MgSO$_4$. The organic layers were concentrated
to afford 316 mg of a crude residue in quantitative yield, which was purified
by silica gel column chromatography (CH$_2$Cl$_2$) to afford pure benzothiophene
chlorobenzyl carboxamide (7) (272 mg, 86%) as a viscous orange-brown oil.
Anal. calcd. for C$_{18}$H$_{16}$NO$_3$SCl: C, 59.75; H, 4.46; N, 3.87; S, 8.86. Found: C,
55.89; H, 4.48; N, 3.77; S, 8.82%; IR $v_{max}$: 3417 (ArCONH), 1637 (NHCO),
1575 (N-H). $^1$H NMR (DMSO-d$_6$): $\delta$ 3.93 (s, 6H, 2Ar-OMe), 4.88 (s, 2H,
Ar-CH$_2$-Cl), 6.91 (d, 1H, 5-H, $J$ = 8.5 Hz), 6.99 (d, 1H, 6-H, $J$ = 8.5 Hz),
7.32 (t, 1H, 4’-H, $J$ = 6.3 Hz), 7.42–7.49 (m, 2H, 5’-H and 6’-H), 7.55
(d, 1H, 3’-H, $J$ = 7.5 Hz), 9.15 (s, 1H, 3-H), 10.30 (s, 1H, NH-CO). $^1$C
NMR (75 MHz, CDCl$_3$): $\delta$ 44.6, 55.8, 56.1, 104.8, 106.6, 122.9, 124.3,
125.3, 127.8, 130.0, 130.2, 131.4, 132.0, 134.6, 137.7, 148.5, 150.3, 160.8.

General Procedure for Preparation of 4,7-Dimethoxy-N-[2-[(4-aryl-
1-piperazinyl) methyl] phenyl]benzo[b]thiophene-2-
carboxamides 8 (a–f)

4,7-Dimethoxy-N-[2-[(4-phenyl-1-piperazinyl)-methyl]phenyl]
benzo[b]thiophene-2-carboxamide (8a)

To a solution of chlorobenzyl benzo[b]thiophene (7) (105 mg, 0.29 mmol) in
CH$_3$CN (20 mL), 1-phenyl piperazine (48 mg, 0.29 mmol) and anhydrous
K$_2$CO$_3$ (40 mg, 0.29 mmol) were added. The mixture was stirred under reflux
for 4 h and then diluted with water (50 mL). The solution was extracted with
ethyl acetate (40 mL × 3), and the organic layers were dried over anhydrous
Na$_2$SO$_4$. Removal of the solvent afforded benzo[b]thiophene-2-carboxamide
(8a) (136 mg, 96%) as a white powder, which was purified by silica-gel column
chromatography (CH$_2$Cl$_2$) (116 mg, 82%). Mp: 206–207°C (CH$_2$Cl$_2}$/CH$_3$CN 1:2).
Anal. calcd. for C$_{28}$H$_{29}$N$_3$O$_3$S: C, 68.97; H, 5.99; N, 8.62; S, 6.58. Found: C,
68.48; H, 5.90; N, 8.60; S, 6.38%. IR $v_{max}$: 3450 (ArCONH), 3032 (C-H, Ar), 1666 (NHC=O), 1595 (N-H). $^1$H NMR
(300 MHz, CDCl₃) δ: 2.75 (bs, 4H, Piper. 2”-H and 6”-H), 3.41 (bs, 4H, Piper. 3”-H and 5”-H), 3.58 (s, 3H, Ar-OMe, C-7), 3.74 (s, 2H, Ar-CH₂-), 3.92 (s, 3H, Ar-OMe, C-4), 6.59 (d, 1H, 5-H, J = 8.5 Hz), 6.71 (d, 1H, 6-H, J = 8.5 Hz), 6.88 (t, 1H, 4”-H, J = 7.3 Hz), 6.97 (d, 2H, 2”-H and 6”-H, J = 8.0 Hz), 7.10 (t, 1H, 5”-H, J = 7.4 Hz), 7.18 (d, 1H, 3”-H, J = 6.5 Hz), 7.27 (dd, 2H, 3”-H, 5”-H, Jₐ = 6.8 Hz, Jₘ = 2.4 Hz), 7.36 (t, 1H, 4’-H, J = 7.6 Hz), 8.10 (s, 1H, 3-H). 13C NMR (75 MHz, CDCl₃): δ 48.9 (2C), 53.0 (2C), 55.2, 56.0, 62.6, 104.4, 106.2, 116.3 (2C), 120.0, 120.9, 121.8, 123.6, 125.0, 128.8, 129.2 (2C), 130.1, 131.4, 132.0, 138.4, 139.8, 148.5, 150.1, 151.2, 160.4.

N-[2-[4-(4-Fluorophenyl)-1-piperazinylmethyl]phenyl]-4,7-dimethoxybenzo[b]thiophene-2-carboxamide (8b)

This is analogous to (8a), prepared from (7) (91 mg, 0.25 mmol), 4-(4-fluorophenyl)piperazine (45 mg, 0.25 mmol), anhydrous K₂CO₃ (35 mg, 0.25 mmol), and CH₃CN (20 mL). Crude yield (94 mg, 74%); column chromatographed (CH₂Cl₂) (79 mg, 62.4%). Mp: 188–189°C. Anal. calcd. for C₂₈H₂₈F₂N₃O₃S: C, 66.51; H, 5.58; N, 8.31; S, 6.34. Found: C, 65.50; H, 5.73; N, 8.51; S, 6.20%. IR νₘₐₓ: 3442 (ArCONH), 3032 (C-H, Ar), 1662 (NHC=O), 1596 (N-H). 1H NMR (300 MHz, CDCl₃): δ: 2.75 (bs, 4H, Piper. 2”-H and 6”-H), 3.33 (bs, 4H, Piper. 3”-H and 5”-H), 3.59 (s, 3H, Ar-OMe, C-7), 3.74 (s, 2H, Ar-CH₂-), 3.92 (s, 3H, Ar-OMe, C-4), 6.50 (d, 1H, 5-H, J = 8.5 Hz), 6.72 (d, 1H, 6-H, J = 8.5 Hz), 7.01–6.90 (m, 4H, 2”-H, 3”-H, 5”-H, 6”-H), 7.06 (t, 1H, 5’-H, J = 6.9 Hz), 7.18 (d, 1H, 3”-H, J = 6.3 Hz), 7.37 (t, 1H, 4’-H, J = 8.0 Hz), 8.10 (s, 1H, 3-H), 8.49 (d, 1H, 6’-H, J = 8.1 Hz), 11.5 (s, 1H, NH-CO). 13C NMR (75 MHz, CDCl₃): δ 49.8 (2C), 52.9 (2C), 55.1, 56.0, 62.5, 104.4, 106.1, 115.6 (d, 2C, J = 22 Hz), 118.02 (d, 2C, J = 7.6 Hz), 120.8, 121.7, 123.6, 124.9, 128.8, 130.1, 131.2, 131.9, 138.4, 139.8, 147.8, 148.5, 149.9, 157.3 (d, J = 239 Hz), 160.3.

N-[2-[4-(2-Fluorophenyl)-1-piperazinyl]methyl]phenyl]-4,7-dimethoxybenzo[b]thiophene-2-carboxamide (8c)

This is analogous to (8a), prepared from (7) (181 mg, 0.5 mmol), 4-(2-fluorophenyl)piperazine (90 mg, 0.5 mmol), anhydrous K₂CO₃ (69 mg, 0.5 mmol), and CH₃CN (20 mL). Crude yield (164 mg, 65%); column chromatographed (CH₂Cl₂) (150 mg, 59%). Mp: 180–181°C. Anal. calcd. for C₂₈H₂₈F₂N₃O₃S: C, 66.51; H, 5.58; N, 8.31; S, 6.34. Found: C, 65.81; H, 5.47; N, 8.29; S, 6.33%. IR νₘₐₓ: 3440 (ArCONH), 1665 (NHC=O), 1592 (N-H). 1H NMR (300 MHz, CDCl₃): δ: 2.75 (m, 4H, Piper. 2”-H and 6”-H), 3.32 (m, 4H, Piper. 3”-H and 5”-H), 3.64 (s, 3H, Ar-OMe, C-7), 3.75 (s, 2H, Ar-CH₂-), 3.92 (s, 3H, Ar-OMe, C-4), 6.61 (d, 1H, 6-H, J = 8.5 Hz), 6.73 (d, 1H, 5-H, J = 8.5 Hz), 6.86–7.10 (m, 5H, 4’-H & 3”-H, 4”-H, 5”-H and 6”-H), 7.18 (dd, 1H, 3’-H, Jₐ = 7.3 Hz, Jₘ = 1.3 Hz), 7.36 (td, 1H, 5’-H, J = 8.3 Hz,
$J_m = 1.35$ Hz), 8.13 (s, 1H, 3-H), 8.42 (dd, 1H, 6'-H, $J_o = 8.2$ Hz, $J_m = 0.8$ Hz), 11.6 (s, 1H, NH-CO). 13C NMR (75 MHz, CDCl$_3$): δ 50.1, 50.2, 53.0, 55.3, 56.0, 62.6, 104.5, 106.2, 116.2 (d, J = 21 Hz), 119.1 (d, J = 2.9 Hz), 120.9, 121.8, 122.7 (d, 2J = 8.0 Hz), 123.7, 124.5, 124.48 (d, 3J = 3.6 Hz), 125.0, 128.8, 130.1, 131.4, 132.0, 138.5, 139.8, 140.0 (d, 2J = 8.6 Hz), 148.6, 150.1, 155.7 (d, 1J = 246 Hz), 160.4.

4,7-Dimethoxy-N-[2-[(4-(2-pyridinyl)-1-piperazinyl)methyl]phenyl]-1-benzo[b]thio-phen-2-carboxamide (8d)

This is analogous to (8a), prepared from (7) (224 mg, 0.62 mmol), 1-(2-pyridinyl) piperazine (101 mg, 0.62 mmol), anhydrous K$_2$CO$_3$ (86 mg, 0.62 mmol), and CH$_3$CN (20 mL). Crude yield (289 mg, 95%); column chromatographed (CH$_2$Cl$_2$) (250 mg, 82.6%). Mp: 186–187°C. Anal. calcd. for C$_{27}$H$_{28}$N$_4$O$_3$S: C, 66.37; H, 5.78; N, 11.47; S, 6.56. Found: C, 65.82; H, 5.85; N, 11.69; S, 6.51%. IR ν$_{max}$: 3438 (ArCONH), 1665 (NHC=O), 1591 (N-H). 1H NMR (300 MHz, CDCl$_3$): δ 2.75 (s, 4H, 2-H and 6-H), 3.68 (s, 3H, Ar-OMe), 3.70–3.79 (m, 6H, Ar-CH$_2$- and Piper. 3-H and 5-H), 3.92 (s, 3H, Ar-OMe), 6.58–6.72 (m, 4H, 5-H, 6-H, and 4'-H & 6'-H), 7.06 (td, 1H, 5-H, $J_o = 6.9$ Hz; 6-H, $J_m = 1.0$ Hz), 7.18 (d, 1H, 3'-H, $J = 6.2$ Hz), 7.49 (td, 1H, 4'-H, $J_o = 7.94$; 3'-H, $J_m = 1.95$ Hz), 7.37 (td, 1H, 4'-H, $J_o = 7.95$; 3'-H, $J_m = 1.43$ Hz), 8.11 (s, 1H, 3-H), 8.22 (dd, 1H, 3'-H, $J_o = 4.78$ Hz; 6'-H, $J_m = 1.38$ Hz), 8.42 (d, 1H, 3''-H, $J = 7.6$ Hz), 11.5 (s, 1H, NH-CO). 13C NMR (75 MHz, CDCl$_3$): δ 44.9 (2C), 52.8 (2C), 55.3, 56.0, 62.7, 104.4, 106.2, 107.1, 113.7, 120.7, 121.7, 123.6, 124.9, 128.8, 130.1, 131.3, 132.0, 137.6, 138.5, 139.8, 148.0, 148.5, 150.1, 159.5, 160.4.

4,7-Dimethoxy-N-[2-[(4-(4-nitrophenyl)-1-piperazinyl)methyl]phenyl]-1-benzo[b]thio-phen-2-carboxamide (8e)

This is analogous to (8a), prepared from (7) (100 mg, 0.28 mmol), 1-(4-nitrophenyl) piperazine (58 mg, 0.24 mmol), anhydrous K$_2$CO$_3$ (38 mg, 0.28 mmol), and CH$_3$CN (20 mL). Crude yield (115 mg, 78.3%); column chromatographed (CH$_2$Cl$_2$) (108 mg, 73.6%). Mp: 244–245°C. Anal. calcd. for C$_{28}$H$_{28}$N$_4$O$_5$S: C, 63.14; H, 5.30; N, 10.52; S, 6.02. Found: C, 62.87; H, 5.59; N, 10.46; S, 5.97%. IR ν$_{max}$: 3445 (ArCONH), 1667 (NHC=O), 1595 (NO$_2$ asym.), 1324 (NO$_2$ sym.). 1H NMR (300 MHz, DMSO-d$_6$): δ 2.76 (bs, 4H, 2'-H and 6'-H), 3.73 (bs, 4H, 3''-H and 5''-H), 3.85 (s, 3H, Ar-OMe, C-7), 3.93 (s, 3H, OMe, C-4), 3.74 (s, 2H, Ar-CH$_2$-), 6.95 (d, 1H, 5-H, $J = 8.4$ Hz), 7.07 (d, 1H, 6-H, $J = 8.4$ Hz), 7.24–7.40 (m, 3H, 2''-H, 6''-H and 4'-H), 7.54–7.65 (m, 2H, 3'-H and 5'-H), 8.32 (d, 1H, 6'-H, $J = 9.2$ Hz), 8.35 (s, 1H, 3-H), 8.47 (d, 2H, 3''-H and 5''-H, $J = 8.1$ Hz), 11.6 (s, 1H, NHCO). 13C NMR (75 MHz, DMSO-d$_6$): 47.0 (2C), 52.7 (2C), 56.5, 57.0, 61.6, 106.7, 108.4, 113.7 (2C), 121.3, 122.1, 122.3, 124.7, 126.5 (2C), 126.8, 129.0, 131.1, 131.5, 138.3, 138.8, 140.1, 148.8, 150.5, 155.6, 160.3.
4,7-Dimethoxy-N-[2-{(4-(2-methoxyphenyl)-1-piperazinyl)methyl}phenyl]-1-benzo[b]thiophene-2-carboxamide (8f)

This is analogous to (8a), prepared from (7) (140 mg, 0.39 mmol), 1-(2-methoxyphenyl)piperazine (75 mg, 0.39 mmol), anhydrous K2CO3 (54 mg, 0.39 mmol), and CH3CN (20 mL). Crude yield (156 mg, 78%); column chromatographed (CH2Cl2) (148 mg, 74%). Mp: 170–171°C. Anal. calcd. for C29H31N3O4S: C, 67.29; H, 6.04; N, 8.12; S, 6.19. Found: C, 67.26; H, 6.11; N, 7.95; S, 6.02%. IR νmax: 3441 (ArCONH), 1660 (NHC5-O), 1590 (N-H). 1H NMR (300 MHz, CDCl3): δ 2.76 (bs, 4H, 2-H and 6-H), 3.29 (bs, 4H, 3-H and 5-H), 3.65 (s, 3H, Ar-OMe), 3.75 (s, 2H, Ar-CH2-), 3.88 (s, 3H, Ar-OMe, 7-H), 3.96 (s, 3H, Ar-OMe, 4-H), 6.62 (d, 1H, 5-H, J = 8.4 Hz), 6.73 (d, 1H, 6-H, J = 8.4 Hz), 6.84–7.09 (m, 5H, 5-H and 3-H, 4′-H, 5′-H & 6′-H), 7.18 (d, 1H, 3-H, J = 6.9 Hz), 7.35 (t, 1H, 4′-H, J = 7.0 Hz), 8.16 (s, 1H, 3-H), 8.40 (d, 1H, 6′-H, J = 8.2 Hz), 11.6 (s, 1H, CONH). 13C NMR (75 MHz, CDCl3): 50.7 (2C), 53.6 (2C), 55.7, 55.8, 56.4, 63.1, 104.8, 106.6, 111.7, 118.8, 121.3, 121.4, 122.2, 123.9, 123.5, 125.6, 129.1 (2C), 130.4, 131.8, 138.9, 140.3, 141.6, 148.9, 150.3, 152.7, 160.8.

ACKNOWLEDGMENTS

We thank Proyectos Fondecyt 1050289 and Proyecto Cepedeq-Facultad, Facultad de Ciencias Químicas y Farmacêuticas Universidad de Chile, Santiago, Chile.

REFERENCES


